EXHIBIT B - FILE WRAPPER DOCUMENT CORRESPONDING TO HEADING "APPLICANT ARGUMENTS/REMARKS MADE IN AN AMENDMENT"

AMENDMENTS TO THE SPECIFICATION

Please amend the first paragraph of the specification, page 1, lines 3-4, as follows:

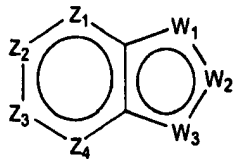
~~This application claims the benefit of priority of copending U.S. Provisional Application Serial Number 60/200/791, filed April 28, 2000.~~

This application is a divisional of U.S. Patent Application Serial No. 09/844,685, entitled "MUSCARINIC AGONISTS," filed April 27, 2001, now U.S. Patent No. 6,627,645, issued September 30, 2003, by Andersson, et al., which in turn claims priority to U.S. Provisional Patent Application Serial No. 60/200,791, filed April 28, 2000, all of which are incorporated by reference herein in their entirety, including any drawings.

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

1. (CURRENTLY AMENDED) A compound of formula (I):



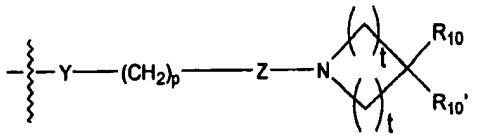
(I)

wherein:

Z_1 is CR_1 ~~or N~~, Z_2 is CR_2 ~~or N~~, Z_3 is CR_3 ~~or N~~, and Z_4 is CR_4 ~~or N, where no more than two of Z_1, Z_2, Z_3 and Z_4 are N~~;

W_1 is O~~;~~ or S, ~~or NR_5; one of~~ W_2 ~~and W_3~~ is N or CR_6, and ~~the other of W_2 and~~ W_3 is CG; ~~W_1 is NG, W_2 is CR_5 or N, and W_3 is CR_6 or N; or W_1 and W_3 are N, and W_2 is NG~~;

G is of formula (II):



(II)

Y is O, S, CHOH, -NHC(O)-, -C(O)NH-, -C(O)-, -OC(O)-, -(O)CO-, $-NR_7$-, -CH=N-, or absent;

p is 1, 2, 3, 4 or 5;

Z is CR_8R_9 or absent;

each t is 1, 2, or 3;

each R_1, R_2, R_3, and R_4, independently, is H, amino, hydroxyl, halo, or straight- or branched-chain C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} heteroalkyl, C_{1-6} haloalkyl, -CN, $-CF_3$, $-OR_{11}$, $-COR_{11}$, $-NO_2$, $-SR_{11}$, $-NHC(O)R_{11}$, $-C(O)NR_{12}R_{13}$, $-NR_{12}R_{13}$, $-NR_{11}C(O)NR_{12}R_{13}$, $-SO_2NR_{12}R_{13}$, $-OC(O)R_{11}$, $-O(CH_2)_qNR_{12}R_{13}$, or $-(CH_2)_qNR_{12}R_{13}$, where q is an integer from 2 to 6, or R_1 and R_2 together form -NH-N=N- or R_3 and R_4 together form -NH-N=N-;

each R_5, R_6, and R_7, independently, is H, C_{1-6} alkyl; formyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl;

each R_8 and R_9, independently, is H or straight- or branched-chain C_{1-8} alkyl;

R_{10} is H, straight- or branched-chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8} hydroxyalkoxy, C_{1-8} hydroxyalkyl, -SH, C_{1-8} alkylthio, -O-CH_2-C_{5-6} aryl, -C(O)-C_{5-6} aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} cycloalkyl, C_{5-6} heteroaryl, C_{5-6} heterocycloalkyl, -$NR_{12}R_{13}$, -$C(O)NR_{12}R_{13}$, -$NR_{11}C(O)NR_{12}R_{13}$, -$CR_{11}R_{12}R_{13}$, -$OC(O)R_{11}$, -$(O)(CH_2)_sNR_{12}R_{13}$ or -$(CH_2)_sNR_{12}R_{13}$, s being an integer from 2 to 8;

R_{10}' is H, straight- or branched-chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8} hydroxyalkoxy, C_{1-8} hydroxyalkyl, or C_{1-8} alkylthio;

each R_{11}, independently, is H, straight- or branched-chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{2-8} heteroalkyl, C_{2-8} aminoalkyl, C_{2-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{2-8} hydroxyalkyl, -C(O)-C_{5-6} aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} heteroaryl, C_{5-6} cycloalkyl, C_{5-6} heterocycloalkyl, -$C(O)NR_{12}R_{13}$, -$CR_5R_{12}R_{13}$, -$(CH_2)_tNR_{12}R_{13}$, t is an integer from 2 to 8; and

each R_{12} and R_{13}, independently, is H, C_{1-6} alkyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl; or R_{12} and R_{13} together form a cyclic structure;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

2. (ORIGINAL) The compound of claim 1, wherein each t is 2 and R_{10} is straight- or branched-chain C_{2-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, or C_{1-8} heteroalkyl.

3. (ORIGINAL) The compound of claim 2, wherein R_{10} is n-butyl.

4. (CANCELED)

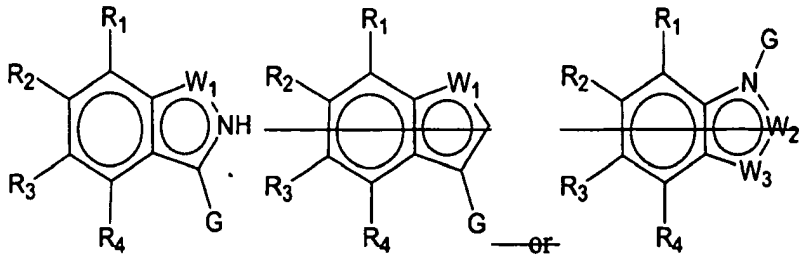
5. (CURRENTLY AMENDED) The compound of claim 4, wherein each R_1, R_2, R_3, and R_4, independently, is H, hydroxyl, halo, C_{1-6}heteroalkyl, CF_3, -NO_2, or straight- or branched-chain C_{1-6} alkyl, or R_1 and R_2 together form -NH-N=N- or R_3 and R_4 together form -NH-N=N-.

6. (ORIGINAL) The compound of claim 2, wherein Y is absent or O, p is 0, 1, 2 or 3, and R_8 and R_9 are H.

7. (ORIGINAL) The compound of claim 6, wherein Z is absent, Y is absent and p is 3.

8. (ORIGINAL) The compound of claim 7, wherein R_{10} is n-butyl.

9. (ORIGINAL) The compound of claim 2, wherein the compound is of the formula



wherein W_1 is O, or S, ~~or NR_5, W_2 is CR_5 or N, and W_3 is CR_5 or N~~.

10. (ORIGINAL) The compound of claim 9, wherein Z is absent, Y is absent and p is 3.

11. (ORIGINAL) The compound of claim 10, wherein R_{10} is n-butyl.

12. (ORIGINAL) The compound of claim 9, wherein R_5 is H or $C_{1\text{-}6}$ alkyl.

13 - 16. (CANCELED)

17. (CURRENTLY AMENDED) The compound of claim 1, wherein the compound is:

~~2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-benzothiazole;~~

~~2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-benzooxazole;~~

~~4,5-difluoro-2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-1*H*-benzoimidazole;~~

~~6-fluoro-5-nitro-2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-1*H*-benzoimidazole;~~

~~5-tert-butyl-2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-1*H*-benzoimidazole;~~

~~5-chloro-6-methyl-2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-1*H*-benzoimidazole;~~

~~4,6-difluoro-2-(3-(4-*n*-butylpiperidine-1-yl)-propyl)-1*H*-benzoimidazole;~~

~~2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-imidazo[*4,5-c*]pyridine;~~

~~8-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-9*H*-purine;~~

~~7-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-3,8-dihydro-imidazo[*4',5':3,4*]benzo[*1,2-d*][*1,2,3*]triazole;~~

~~2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-3a,4,5,6,7,7a-hexahydro-1*H*-benzoimidazole;~~

~~1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~3-methyl-1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~5-bromo-1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~3-formyl-1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~7-bromo-1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~1-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indazole;~~

3-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-benzo[*d*]isoxazole;

~~3-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indole;~~

~~4-nitro-2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~5-nitro-2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~4-hydroxy-2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~4-methyl-2-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-benzoimidazole;~~

~~3-(2-(4-*n*-butylpiperidine)-1-yl-ethyl)-1*H*-indole;~~

~~3-(3-(4-*n*-butylpiperidine)-1-yl-propyl)-1*H*-indazole;~~

3-(2-(4-n-butylpiperidine)-ethoxy)-7-methyl-benzo[*d*]isoxazole;

~~1-(3-(4-Methylpiperidine)-1-yl-propyl)-1H-indazole;~~

~~1-(3-(4-Pentylpiperidine)-1-yl-propyl)-1H-indazole;~~

~~1-(3-(4-Propylpiperidine)-1-yl-propyl)-1H-;~~

~~1-(3-(4-(3-Methyl-butyl)-piperidine)-1-yl-propyl)-1H-indazole~~

~~1-(3-(4-Pentylidene-piperidine)-1-yl-propyl)-1H-indazole;~~

~~1-(3-(4-Propylidene-piperidine)-1-yl-propyl)-1H-indazole~~

~~1-Benzo[*b*]thiophen-2-yl-4-(4-butylpiperidin-1-yl)-butan-1-one~~

~~4-(4-Butylpiperidin-1-yl)-1-(3-methyl-benzofuran-2-yl)-butan-1-one;~~

~~4-(4-Butylpiperidin-1-yl)-1-(5-fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-butan-1-one;~~

~~1-Benzofuran-2-yl-4-(4-butylpiperidin-1-yl)-butan-1-one;~~

~~1-(3-Bromo-benzo[*b*]thiophen-2-yl)-4-(4-butylpiperidin-1-yl)-butan-1-one~~

~~1-(3-Benzo[*b*]thiophen-2-yl-propyl)-4-butylpiperidine;~~

~~1-(3-Benzofuran-2-yl-propyl)-4-butylpiperidine;~~

~~4-Butyl-1-[3-(3-methyl-benzofuran-2-yl)-propyl]-piperidine;~~

~~4-Butyl-1-[3-(5-fluoro-3-methyl-benzo[*b*]thiophen-2-yl)-propyl]-piperidine;~~

~~2-(3-Iodo-propyl)-benzo[*b*]thiophene;~~

~~1-(3-Benzo[*b*]thiophen-2-yl-propyl)-4-methylpiperidine~~

~~1-(3-Benzo[*b*]thiophen-2-yl-propyl)-4-benzylpiperidine;~~

~~1-(3-Benzo[*b*]thiophen-2-yl-propyl)-4-(2-methoxy-phenyl)-piperidine;~~

~~2-(3-Bromopropyl)-2H-benzotriazole;~~

~~2-[3-(4-Butylpiperidin-1-yl)-propyl]-2H-benzotriazole;~~

~~1-(3-Bromopropyl)-1H-benzotriazole;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-1H-benzotriazole;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-1*H*-indole-3-carbaldehyde;~~

~~{1-[3-(4-Butylpiperidin-1-yl)-propyl]-1H-indol-3-yl}-methanol;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-2-phenyl-1*H*-benzoimidazole;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-3-chloro-1*H*-indazole;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-6-nitro-1*H*-indazole;~~

~~Benzo[*d*]isoxazol-3-ol;~~

3-(2-Chloroethoxy)-benzo[*d*]isoxazole;

3-[2-(4-Butylpiperidin-1-yl)-ethoxy]-benzo[*d*]isoxazol;

~~3-(1H-Indol-3-yl)-propan-1-ol;~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1*H*-indole hydrochloride;~~

~~4-(4-Butylpiperidine-1-yl)-butyric acid methyl ester;~~

~~2-[3-(4-Butylpiperidin-1-yl)-propyl]-1-methyl-1H-benzimidazole;~~

~~1H-Indazole-3-carboxylic acid (2-(4-butylpiperidin)-1-yl-ethyl)-amide;~~

~~1-[3-(4-Butylpiperidin-1-yl)-propyl]-5-nitro-1H-indazole;~~

~~2-[3-(4-butylpiperidin-1-yl)-propyl]-5-nitro-2H-indazole;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-2-methyl-1*H*-indole;~~

~~1-{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indol-3-yl}-ethanone;~~

~~{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indol-3-yl}-acetonitrile;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1*H*-indole-3-carbonitrile;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5,6-dimethyl-1*H*-benzoimidazole;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5(6)-dimethyl-1*H*-benzoimidazole;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-5-methoxy-1*H*-benzoimidazole;~~

~~{1-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-benzoimidazol-2-yl}-methanol;~~

~~1-[3-(4-Butyl-piperidin-1-yl)-propyl]-2-trifuoromethyl-1*H*-benzoimidazole;~~

~~(2-Trimethylstannanyl-phenyl)-carbamic acid *tert*-butyl ester;~~

~~[2-(4-Chloro-butyryl)-phenyl]-carbamic acid *tert*-butyl ester;~~

~~{2-[4-(4-Butyl-piperidine-1-yl)-butyryl]-phenyl}-carbamic acid *tert*-butyl ester;~~

~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-1H-indazole, HCl;~~

~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-5-nitro-1H-indazole;~~

~~3-[3-(4-Butyl-piperidine-1-yl)-propyl]-5,7-dinitro-1H-indazole;~~

~~4-(4-Butyl-piperidin-1-yl)-1-(2-metylsulfanyl-phenyl)-butan-1-one;~~

or 3-[3-(4-Butyl-piperidin-1-yl)-propyl]-benzo[*d*]isothiazole.~~;~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-5-methoxy-1H-indazole;~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-4-methoxy-1H-indazole~~

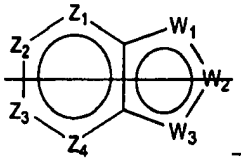
~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-6-methoxy-1H-indazole;~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-4-ol (53MF51);~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-6-ol (53MF52); or~~

~~3-[3-(4-Butyl-piperidin-1-yl)-propyl]-1H-indazole-5-ol.~~

18. (CURRENTLY AMENDED) A pharmaceutical composition comprising an effective amount of a compound of claim 1~~formula (I):~~



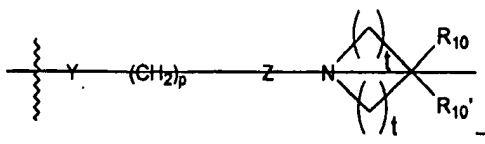
~~(I)~~

~~wherein:~~

~~Z_1 is CR_1 or N, Z_2 is CR_2 or N, Z_3 is CR_3 or N, and Z_4 is CR_4 or N, where no more than two of Z_1, Z_2, Z_3 and Z_4 are N;~~

~~W_1 is O, S, or NR_5, one of W_2 and W_3 is N or CR_6, and the other of W_2 and W_3 is CG; W_1 is NG, W_2 is CR_5 or N, and W_3 is CR_6 or N; or W_1 and W_3 are N, and W_2 is NG;~~

~~G is of formula (II):~~



~~(II)~~

~~Y is O, S, CHOH, NHC(O), C(O)NH, C(O), OC(O), (O)CO, NR_4, CH=N, or absent;~~

~~p is 1, 2, 3, 4 or 5;~~

~~Z is CR_8R_9 or absent;~~

~~each t is 1, 2, or 3;~~

~~each R_1, R_2, R_3, and R_4, independently, is H, amino, hydroxyl, halo, or straight or branched chain C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} heteroalkyl, C_{1-6} haloalkyl, CN, CF_3, OR_{11}, COR_{11}, NO_2, SR_{11}, $NHC(O)R_{11}$, $C(O)NR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{11}C(O)NR_{12}R_{13}$, $SO_2NR_{12}R_{13}$, $OC(O)R_{11}$, $O(CH_2)_qNR_{12}R_{13}$, or $(CH_2)_qNR_{12}R_{13}$, where q is an integer from 2 to 6, or R_1 and R_2 together form $-NH-N=N-$ or R_3 and R_4 together form $-NH-N=N-$;~~

~~each R_5, R_6, and R_7, independently, is H, C_{1-6} alkyl; formyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl;~~

~~each R_8 and R_9, independently, is H or straight or branched chain C_{1-8} alkyl;~~

~~R_{10} is straight or branched chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8} hydroxyalkoxy, C_{1-8} hydroxyalkyl, SH, C_{1-8} alkylthio, O CH_2 C_{5-6} aryl, C(O) C_{5-6} aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} cycloalkyl, C_{5-6} heteroaryl, C_{5-6} heterocycloalkyl, $NR_{12}R_{13}$, $C(O)NR_{12}R_{13}$, $NR_{11}C(O)NR_{12}R_{13}$, $CR_{11}R_{12}R_{13}$, $OC(O)R_{11}$, $(O)(CH_2)_sNR_{12}R_{13}$ or $(CH_2)_sNR_{12}R_{13}$, s being an integer from 2 to 8;~~

~~R_{10}' is H, straight or branched chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8} hydroxyalkoxy, C_{1-8} hydroxyalkyl, or C_{1-8} alkylthio;~~

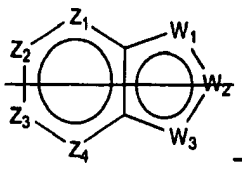
~~each R_{11}, independently, is H, straight or branched chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{2-8} heteroalkyl, C_{2-8} aminoalkyl, C_{2-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{2-8} hydroxyalkyl, C(O) C_{5-6} aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} heteroaryl, C_{5-6} cycloalkyl, C_{5-6} heterocycloalkyl, $C(O)NR_{12}R_{13}$, $CR_5R_{12}R_{13}$, $(CH_2)_tNR_{12}R_{13}$, t is an integer from 2 to 8; and~~

~~each R_{12} and R_{13}, independently, is H, C_{1-6} alkyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl; or R_{12} and R_{13} together form a cyclic structure;~~

~~or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

19 –34. (CANCELED)

35. (CURRENTLY AMENDED) A method of increasing an activity of a cholinergic receptor comprising contacting the cholinergic receptor or a system containing the cholinergic receptor with an effective amount of at least one compound of claim 1. ~~formula (I):~~



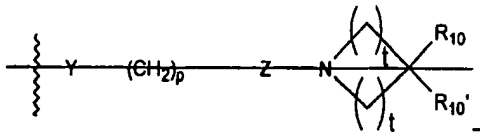
~~(I)~~

~~wherein:~~

~~Z_1 is CR_1 or N, Z_2 is CR_2 or N, Z_3 is CR_3 or N, and Z_4 is CR_4 or N, where no more than two of Z_1, Z_2, Z_3 and Z_4 are N;~~

~~W_1 is O, S, or NR_5, one of W_2 and W_3 is N or CR_6, and the other of W_2 and W_3 is CG; W_1 is NG, W_2 is CR_5 or N, and W_3 is CR_6 or N; or W_1 and W_3 are N, and W_2 is NG;~~

~~G is of formula (II):~~



~~(II)~~

~~Y is O, S, CHOH, NHC(O), C(O)NH, C(O), OC(O), (O)CO, NR_7, CH=N, or absent;~~

~~p is 1, 2, 3, 4 or 5;~~

~~Z is CR_8R_9 or absent;~~

~~each t is 1, 2, or 3;~~

~~each R_1, R_2, R_3, and R_4, independently, is H, amino, hydroxyl, halo, or straight or branched chain C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} heteroalkyl, C_{1-6} haloalkyl, CN, CF_3, OR_{11}, COR_{11}, NO_2, SR_{11}, $NHC(O)R_{11}$, $C(O)NR_{12}R_{13}$, $NR_{12}R_{13}$, $NR_{11}C(O)NR_{12}R_{13}$, $SO_2NR_{12}R_{13}$, $OC(O)R_{11}$, $O(CH_2)_qNR_{12}R_{13}$, or $(CH_2)_qNR_{12}R_{13}$, where q is an integer from 2 to 6, or R_1 and R_2 together form NH-N=N or R_3 and R_4 together form NH-N=N;~~

~~each R_5, R_6, and R_7, independently, is H, C_{1-6} alkyl; formyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl;~~

~~each R_8 and R_9, independently, is H or straight or branched chain C_{1-8} alkyl;~~

~~R_{10} is straight or branched chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8}~~

~~hydroxyalkoxy, C_{1-8} hydroxyalkyl, SH, C_{1-8} alkylthio, $O\text{-}CH_2\text{-}C_{5-6}$ aryl, $C(O)\text{-}C_{5-6}$ aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} cycloalkyl, C_{5-6} heteroaryl, C_{5-6} heterocycloalkyl, $NR_{12}R_{13}$, $C(O)NR_{12}R_{13}$, $NR_{11}C(O)NR_{12}R_{13}$, $CR_{11}R_{12}R_{13}$, $OC(O)R_{11}$, $(O)(CH_2)_sNR_{12}R_{13}$ or $(CH_2)_sNR_{12}R_{13}$, s being an integer from 2 to 8;~~

~~R_{10}' is H, straight- or branched-chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} alkylidene, C_{1-8} alkoxy, C_{1-8} heteroalkyl, C_{1-8} aminoalkyl, C_{1-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{1-8} hydroxyalkoxy, C_{1-8} hydroxyalkyl, or C_{1-8} alkylthio;~~

~~each R_{11}, independently, is H, straight- or branched-chain C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{2-8} heteroalkyl, C_{2-8} aminoalkyl, C_{2-8} haloalkyl, C_{1-8} alkoxycarbonyl, C_{2-8} hydroxyalkyl, $C(O)\text{-}C_{5-6}$ aryl substituted with C_{1-3} alkyl or halo, C_{5-6} aryl, C_{5-6} heteroaryl, C_{5-6} cycloalkyl, C_{5-6} heterocycloalkyl, $C(O)NR_{12}R_{13}$, $CR_5R_{12}R_{13}$, $(CH_2)_tNR_{12}R_{13}$, t is an integer from 2 to 8; and~~

~~each R_{12} and R_{13}, independently, is H, C_{1-6} alkyl; C_{3-6} cycloalkyl; C_{5-6} aryl, optionally substituted with halo or C_{1-6} alkyl; or C_{5-6} heteroaryl, optionally substituted with halo or C_{1-6} alkyl; or R_{12} and R_{13} together form a cyclic structure;~~

~~or a pharmaceutically acceptable salt, ester or prodrug thereof.~~

36. (ORIGINAL) The method of claim 35 wherein the cholinergic receptor is a muscarinic receptor.

37. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is of the m1 muscarinic receptor subtype.

38. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is of the m4 muscarinic receptor subtype.

39. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the central nervous system.

40. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the peripheral nervous system.

41. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is in the gastrointestinal system, heart, endocrine glands, or lungs.

42. (ORIGINAL) The method of claim 36 wherein the muscarinic receptor is truncated, mutated, or modified.

43. (ORIGINAL) The method of claim 35 wherein the activity is a signaling activity of a cholinergic receptor.

44. (ORIGINAL) The method of claim 35 wherein the activity is associated with muscarinic receptor activation.

45. (ORIGINAL) The method of claim 35 wherein the compound is a cholinergic agonist.

46. (ORIGINAL) The method of claim 35 wherein the compound is selective for the m1, or m4 muscarinic receptor subtype, or both the m1 and m4 muscarinic receptor subtypes.

47. (ORIGINAL) A method of activating a cholinergic receptor comprising contacting the cholinergic receptor or a system containing the cholinergic receptor with an effective amount of at least one compound of claim 1.

48 - 55. (CANCELED)

56. (CURRENTLY AMENDED) A method of treating a disease condition ~~associated with~~ caused by a cholinergic receptor comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

57. (ORIGINAL) The method of claim 56 wherein the disease condition is selected from the group consisting of cognitive impairment, forgetfulness, confusion, memory loss, attentional deficits, deficits in visual perception, depression, pain, sleep disorders, psychosis, hallucinations, aggressiveness, paranoia, ~~and~~ increased intraocular pressure, neurodegenerative disease, Alzheimer's disease, Parkinson's disease, Huntington's chorea, Friederich's ataxia, Gilles de la Tourette's Syndrome, Down Syndrome, Pick disease, dementia, clinical depression, age-related cognitive decline, attention-deficit disorder, sudden infant death syndrome, and glaucoma.

58. (CANCELED)

59. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by a cholinergic receptor dysfunction.

60. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by decreased activity of a cholinergic receptor.

61. (CURRENTLY AMENDED) The method of claim 56 wherein the disease condition is ~~associated with~~ caused by loss of cholinergic receptors.

62 - 67. (CANCELED)

68. (ORIGINAL) A method of treating a disease condition associated with reduced levels of acetylcholine comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

69. (CURRENTLY AMENDED) A method of treating a condition selected from the group consisting of Alzheimer's Disease cognitive impairment, glaucoma, pain, and schizophrenia, comprising administering to a subject in need of such treatment an effective amount of at least one compound of claim 1.

70 – 73. (CANCELED)

74. (ORIGINAL) A method for identifying a genetic polymorphism predisposing a subject to being responsive to amount of at least one compound of claim 1, comprising:

administering to a subject an therapeutically effective amount of the compound;

measuring the response of said subject to said compound, thereby identifying a responsive subject having an ameliorated disease condition associated with a cholinergic receptor; and

identifying a genetic polymorphism in the responsive subject, wherein the genetic polymorphism predisposes a subject to being responsive to the compound.

75. (ORIGINAL) The method of claim 74 wherein the ameliorated disease condition is associated with the m1 or m4 muscarinic receptor subtype.

76. (ORIGINAL) A method for identifying a subject suitable for treatment with at least one compound of claim 1, comprising detecting the presence of a polymorphism in a subject wherein the polymorphism predisposes the subject to being responsive to said compound, and wherein the presence of the polymorphism indicates that the subject is suitable for treatment with said compound of claim 1.

REMARKS

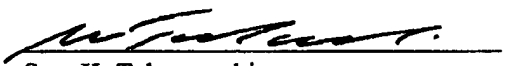
By present amendments, Applicants have incorporated into the specification a paragraph indicating that the present application is a divisional of a pending U.S. application, to which the present application claims priority. In addition, In this divisional application, Applicants are pursuing subject matter drawn to benzisoxazole and benzisothiazole compounds. Applicants have canceled the subject matter drawn to other unelected groups. Cancellation of the claims or the subject matter makes no admission as to the patentability thereof, and therefore, should not be so construed. Applicants reserve the right to pursue the canceled subject matter in this or any other continuation, divisional, or continuation-in-part application.

Applicants believe that the claims as presented herein are patentable and a notice to that effect is respectfully requested. No fee is believed due in connection with this preliminary amendment. However, if this is incorrect, the Director is hereby authorized to charge any necessary fees to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Sept. 24, 2003

By: 

Sam K. Tahmassebi
Registration No. 45,151
Attorney of Record
Customer No. 20,995
(619) 235-8550

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